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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,436	02/10/2005	Jurgen Schulein	GAS-002	5715
32628 7	590 01/03/2006		EXAMINER	
	BERNER AND PAI	NOGUEROLA, ALEXANDER STEPHAN		
	SUITE 300, 1700 DIAGONAL RD ALEXANDRIA, VA 22314-2848		ART UNIT	PAPER NUMBER
	,		1753	

DATE MAILED: 01/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)			
	10/517,436	SCHULEIN ET AL.			
Office Action Summary	Examiner	Art Unit			
	ALEX NOGUEROLA	1753			
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the	correspondence address			
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication.  If NO period for reply is specified above, the maximum statutory period versilled to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be ting will apply and will expire SIX (6) MONTHS from a cause the application to become ABANDONE	N. mely filed the mailing date of this communication. ED (35 U.S.C. § 133).			
Status					
1) Responsive to communication(s) filed on 10/25	5/2005.				
·- ·	action is non-final.				
3) Since this application is in condition for allowar	nce except for formal matters, pro	osecution as to the merits is			
closed in accordance with the practice under E	x parte Quayle, 1935 C.D. 11, 4	53 O.G. 213.			
Disposition of Claims					
4) Claim(s) 1-9 and 11-13 is/are pending in the ap	oplication.				
4a) Of the above claim(s) is/are withdrawn from consideration.					
5) Claim(s) is/are allowed.					
6)⊠ Claim(s) <u>1-9 and 11-13</u> is/are rejected.					
7) Claim(s) is/are objected to.					
8) Claim(s) are subject to restriction and/or	r election requirement.				
Application Papers					
9) The specification is objected to by the Examine	r.				
10)⊠ The drawing(s) filed on <u>10 December 2004</u> is/are: a)⊠ accepted or b)  objected to by the Examiner.					
Applicant may not request that any objection to the					
Replacement drawing sheet(s) including the correct	•				
11) The oath or declaration is objected to by the Ex	aminer. Note the attached Office	e Action or form PTO-152.			
Priority under 35 U.S.C. § 119					
12) Acknowledgment is made of a claim for foreign	priority under 35 U.S.C. § 119(a	)-(d) or (f).			
a) All b) Some * c) None of:	s have been received				
<ul> <li>1. Certified copies of the priority documents have been received.</li> <li>2. Certified copies of the priority documents have been received in Application No</li> </ul>					
3. Copies of the certified copies of the prior					
application from the International Bureau	•				
* See the attached detailed Office action for a list		ed.			
Attachment(s)					
1) Notice of References Cited (PTO-892)  2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	4)  Interview Summary Paper No(s)/Mail D				
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)	5) 🔲 Notice of Informal F	Patent Application (PTO-152)			
Paper No(s)/Mail Date	6)				

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#### **DETAILED ACTION**

#### Response to Amendment

1. Applicants' amendment of October 25, 2005 ("Amendment") does not render the application allowable.

### Response to Arguments

#### 35 U.S.C. §102(e) - Hashimoto

#### 2. Applicants assert

The circuit disclosed in Hasimoto's Fig. 15 has several disadvantages. For detecting the current via the working electrode, the drop in voltage across the resistor  $R_{\rm f}$  is measured. As the drop in voltage is dependent on the current flowing through the respective working electrode, it follows that the working electrode cannot be at the potential during the measurement.

In contrast, according to the Applicant's claimed invention, all of the working electrodes are connected to the virtual ground, and are therefore held at the same potential. this significantly simplifies the measurement. Page 11 of Amendment.

However, Hashimoto states, "The largeness of the current [caused by applying the voltage to the nucleic acid fixed chain electrode 1601] can be measured by

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measuring the voltage down by the resistor **1610.**" See col. 16:6-12. The examiner has not found were Hashimoto discloses detecting the current via the working electrode by measuring the voltage drop across resistor R<sub>f</sub>. As seen in Fig. 15, resistor R<sub>f</sub> at best indicates the current flow between counter electrode **1602** and reference electrode **1603**. Furthermore, Hashimoto states, "Since the potential of the nucleic acid chain fixed electrode **1601** is equal to the <u>potential of common</u>, an equal voltage to the input voltage is accurate applied between the nucleic acid chain fixed electrode **1601** (action electrode) and the reference electrode **1603** [emphasis added]." See col. 16:1-6. Thus the working electrodes in Hashimoto are connected to virtual ground

Applicants also state,

Even if one were to assume that the resistance across  $R_f$  shown in Hashimoto's Fig. 15 is very small, and that the working electrodes could be considered to be at approximately the same potential, then it would be necessary to provide an extremely precise differential amplifier for the measurement of the current. Such a measurement will be susceptible to error from noise. *Page 11 of Amendment*.

However, Hashimoto states, "These circuits [operation amplifier circuits in Fig. 15] are different from conventional circuit in the point for the <u>minute current measurement</u>. Therefore, the pontiostat circuit used in the nucleic acid detection sensor may be a circuit for the <u>minute current measurement</u> [emphasis added]." See col. 15:26-32. That is, a special feature of the circuit of Fig. 15 is that it is especially adapted for measuring very small currents.

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#### 35 U.S.C. §103(a) - Hashimoto in view of Blades and Ho

#### Applicants assert

... there is no suggestion or motivation in any of Hashimoto or Blades or Ho that would have led one to select the references and combine them in a way that would produce the invention defined by claim 11. Blades and Ho may disclose the use of a capacitance, but there is no suggestion in any of the references that would have led one to combine their teachings with other references so as to arrive at Applicants' claimed device.

The examiner respectfully disagrees. Blades and Ho are analogous art to Hashimoto. As stated on page 11 of the Office action of July 25, 2005 ('Office action"), "Ho and Blades discloses measuring circuits for electrochemical measuring cells …" As also stated on page 11 of the Office action, "it would have been obvious to provide such a capacitance [as taught by Ho and Blades] because… as taught by Ho and Blades such a capacitance will smooth the signal to or from the electrode (see in Ho col. 4:49-54 and in Blades col. 5:17-21)."

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# Status of Objections and Rejections pending since the Office action of July 25 2005

- 3. The rejections of claims 1-14 under 35 U.S.C. §112, second paragraph, are withdrawn.
- 4. The rejections of claims 1, 2, and 4 under 35 U.S.C. §102(e) as being anticipated by Sampson are withdrawn.
- 5. The rejections of claims 1-10 and 12-14 under 35 U.S.C. §102(e) as being anticipated by Hashimoto are withdrawn.
- 6. The rejection of claim 11 under 35 U.S.C. §103(a) as being obvious over Hashimoto in view of Blades and Ho is withdrawn.

7. The rejections of claims 12-14 under 35 U.S.C. §103(a) as being obvious over Sampson are withdrawn.

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8. The objection to the specification is withdrawn.

#### Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-9, 12, and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Hashimoto et al. (US 6,818,109 B2) ("Hashimoto").

Addressing claim 1, Hashimoto discloses a device for the electrochemical detection of at least one type of a biochemical molecule – contained in a liquid – from a group of predetermined biochemical molecules of different types (abstract), having

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a means (Figures 8A) for taking up the liquid, the means having at least one reference electrode (col. 9:21-26) and at least one counterelectrode (col. 9:4-8) and also more than two working electrodes (Figure 8A), at least in each case one working electrode being provided for the detection of each type of a biochemical molecule (col. 5:6-18), the working electrode being coated with a molecule that is complementary to the biomolecule to be detected also that biochemical molecules of different types can be detected simultaneously (col. 5:6-18 and col. 3:62 – col. 4:5),

a potentiostat (col. 9:49-57) for generating a predetermined voltage profile – which is variable during the measurement (implied since a waveform generator is provided and using a sweeping potential is disclosed. See col.9:49-57 and col. 13:5-22) – between the working electrodes and the reference electrodes, the potentiostat having a third operational amplifier, to whose output the counterelectrode is connected and whose inverting input is connected via a second resistor to an output of a second operational amplifier and is connected via a third resistor to a device for generating a selectable desired voltage, with a noninverting input of the third operational amplifier being grounded (see Figure 15 and note counter electrode 1602, third operational amplifier 1607, second resistor R<sub>f</sub>),

a current/voltage converter (resistor **1610** and amplifier **1609** together in Figure 15. This is implied by col. 16:6-12, which discloses measuring the current across the resistor, which is produced by the working electrode, by measuring the voltage "down" the resistor) being connected downstream of each of the working electrodes (Figure 15), the current/voltage converters holding all of the working electrodes at the

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same potential (this is an intended use; in any event it is implied since one input of amplifier 1609 is grounded) and means for measuring the currents flowing through the working electrodes (implied since measuring current through the working electrode is disclosed. See col. 16:6-12).

Addressing claim 2, for the additional limitation of this claim see col. 4:15-19 and col. 9:21-26.

Addressing claim 3, for the additional limitation of this claim see col. 14:37-42.

Addressing claim 4, for the additional limitation of this claim see col. 9:57-64.

Addressing claim 5, for the additional limitations of this claim see figure 15 and note first operational amplifier **1609**.

Addressing claims 6 and 7, for the additional limitations of these claims see Figure 15. Note that the phrase "it being possible ..." in the claim does not actually require the first resistors to be connected as claimed. In any event, as seen in Figure 15 resistor 1610 is connected in between the amplifier input and the amplifier output.

Addressing claim 8, for the additional limitation of this claim see col. 3:61 – col. 4:5.

Addressing claim 9, for the additional limitations of this claim see Figure 15 and note reference electrode 1603, which is connected to second operational amplifier 1608.

Addressing claim 12, Hashimoto discloses a method for the electrochemical detection of at least one type of a biochemical molecule – contained in a liquid – from a group of predetermined biochemical molecules of different types (abstract), having the following steps

- a) providing a means (Figure 8A) for taking up the liquid, the means having one counter electrode (col. 9:4-8) and a least one reference electrode (col. 9:21-26) and also more than two working electrodes (Figure 8A), at least in each case one working electrode being provided for the detection of each type of a biochemical molecule (col. 5:6-18), the working electrode being coated with a molecule that is complementary to the biomolecule to be detected, so that biochemical molecules of different types can be detected simultaneously (col. 5:6-18 and col. 3:62 col. 5:5),
- b) bringing the liquid into contact with the working, counter-, and reference electrodes (col. 4:34-54),

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c) simultaneously applying a predetermined voltage profile – which is variable during the measurement – between the working electrodes and the reference electrode (implied since a waveform generator is provided and using a sweeping potential is disclosed. See col.9:49-57 and col. 13:5-22), while regulating the voltage between the workgin electrods and the reference electrode with a potentiostate haing a third operational amplifier, to whose output the counterelectrode is connected and whose inverting input is connected via a second resistor to an output of a second operational amplifier and is connected via a third resistor to a device for generating a selectable desired voltage, with a noninverting input of the third operational amplifier being grounded (see col. 9:49-64 and Figure 15 and note counter electrode **1602**, third operational amplifier **1607**, second resistor  $\mathbf{R}_{\mathbf{f}}$ , and

d) measuring the currents flowing through the working electrodes (col. 15:35-45 and col. 16:6-12), all of the working electrodes being held at the same potential during the measurement (col. 9:14-17).

Addressing claim 13, at least multiplexing is disclosed since switching circuits are provided to address the plurality of scanning lines. See col. 5:39.

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#### Claim Rejections - 35 USC § 103

- 11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
  - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 12. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
  - 1. Determining the scope and contents of the prior art.
  - 2. Ascertaining the differences between the prior art and the claims at issue.
  - 3. Resolving the level of ordinary skill in the pertinent art.
  - 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
- 13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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14. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al. (US 6,818,109 B2) ("Hashimoto") in view of Blades (US 5,260,663) ("Blades') and Ho (US 4,488,556) ("Ho").

Hashimoto discloses a device for the electrochemical detection of at least one type of a biochemical molecule – contained in a liquid – from a group of predetermined biochemical molecules of different types (abstract), having

a means (Figures 8A) for taking up the liquid, the means having at least one reference electrode (col. 9:21-26) and at least one counterelectrode (col. 9:4-8) and also more than two working electrodes (Figure 8A), at least in each case one working electrode being provided for the detection of each type of a biochemical molecule (col. 5:6-18), the working electrode being coated with a molecule that is complementary to the biomolecule to be detected also that biochemical molecules of different types can be detected simultaneously (col. 5:6-18 and col. 3:62 – col. 4:5),

a potentiostat (col. 9:49-57) for generating a predetermined voltage profile – which is variable during the measurement (implied since a waveform generator is provided and using a sweeping potential is disclosed. See col.9:49-57 and col. 13:5-22) – between the working electrodes and the reference electrodes, the potentiostat having a third operational amplifier, to whose output the counterelectrode is connected and whose inverting input is connected via a second resistor to an output of a second operational amplifier and is connected via a third resistor to a device for generating a selectable desired voltage, with a noninverting input of the third operational amplifier

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being grounded (see Figure 15 and note counter electrode **1602**, third operational amplifier **1607**, second resistor  $R_f$ ),

a current/voltage converter (resistor **1610** and amplifier **1609** together in Figure 15. This is implied by col. 16:6-12, which discloses measuring the current across the resistor, which is produced by the working electrode, by measuring the voltage "down" the resistor) being connected downstream of each of the working electrodes (Figure 15), the current/voltage converters holding all of the working electrodes at the same potential (this is an intended use; in any event it is implied since one input of amplifier **1609** is grounded) and means for measuring the currents flowing through the working electrodes (implied since measuring current through the working electrode is disclosed. See col. 16:6-12).

As seen in Figure 15 Hashimoto also discloses a counter electrode **1602**, third operational amplifier **1607**, second resistor  $R_{fas}$  claimed.

Hashimoto does not mention providing a capacitance in between the output of the third operational amplifier and the inverting input. Ho and Blades disclose measuring circuits for electrochemical measuring cells comprising a capacitance in between the output of the operational amplifier and the inverting input. It would have been obvious to provide such a capacitance because as taught by Ho and Blades in the invention of Hashimoto because as taught by Ho and Blades such a capacitance will smooth the signal to or from the electrode (see in Ho col. 4:49-54 and in Blades col. 5:17-21).

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## Final Rejection

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola Primary Examiner

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December 28, 2005